Approved Revision: Do Not Implement Until 6/2/21

IncobotulinumtoxinA (Xeomin®)

NDC CODE(S) 00259-1605-XX XEOMIN 50UNIT Solution Reconstituted (MERZ PHARMACEUTICAL)
00259-1610-XX XEOMIN 100UNIT Solution Reconstituted (MERZ PHARMACEUTICAL)
00259-1620-XX XEOMIN 200UNIT Solution Reconstituted (MERZ PHARMACEUTICAL)
46783-0160-xx XEOMIN 100UNIT Solution Reconstituted (MERZ NORTH AMERICA)

DESCRIPTION

Botulinum toxin, produced by the bacterium Clostridium botulinum, is one of the most potent naturally occurring neurotoxins known. It induces chemodenervation by first binding to acceptors on motor nerve terminals. It then enters the terminals and blocks the release of acetylcholine and other neurotransmitters at the neuromuscular junction. This renders smooth and striated muscles incapable of contraction. Acetylcholine also mediates the sympathetic innervation of the sweat glands, explaining how botulinum toxin disrupts the cholinergic outflow to the skin and halts glandular secretion.

The minute amount of toxin used clinically produces only partial, localized chemical denervation with transient results. Over time, axons generate temporary sprouts which release acetylcholine and the original nerve terminal is eventually re-established, ending the toxin's therapeutic activity.

Seven antigenic-specific serotypes of botulinum toxin have been identified, types A, B, C-1, D, E, F and G, but only botulinum toxin types A and B are commercially available. These commercial preparations of the two serotypes (three of serotype A and one of serotype B) vary widely in potency and dosage. They have been given different names to reinforce these differences and to prevent medication errors. It is emphasized that the use and dosage of different formulations of botulinum toxin is not interchangeable.

This policy applies only to incobotulinumtoxinA marketed as Xeomin®.

POLICY

- IncobotulinumtoxinA for the treatment of the following is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
  - Blepharospasms
  - Cervical dystonia
  - Upper limb spasticity
  - Hyperhidrosis, severe primary axillary
  - Overactive bladder
  - Sialorrhea
  - Urinary Incontinence
  - Ventral Hernia
- IncobotulinumtoxinA for the prevention of chronic migraines is considered medically necessary if the medical appropriateness criteria are met. (See Medical Appropriateness below.)
- IncobotulinumtoxinA for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL CRITERIA

- Patient is at least 18 years of age (unless otherwise noted); **AND**

Approved Revision: Do Not Implement Until 6/2/21

Universal Criteria

- Patient evaluated for any disorders which may contribute to respiratory or swallowing difficulty; **AND**
- Patient does not have a hypersensitivity to any botulinum toxin product; **AND**
- Patient does not have an active infection at the proposed injection site; **AND**
- Patient is not on concurrent treatment with another botulinum toxin (i.e., abobotulinumtoxinA, onabotulinumtoxinA, rimabotulinumtoxinB, etc.); **AND**

Cervical Dystonia

- Patient has a history of recurrent involuntary contraction of one or more muscles in the neck; **AND**
  - Patient has sustained head tilt; **OR**
  - Patient has abnormal posturing with limited range of motion in the neck

Blepharospasms

Spastic Conditions

- Patient has one of the following:
  - Upper Limb spasticity in adults (i.e., used post-stroke for spasms)
  - Pediatric upper limb spasticity in patients aged 2 years to 17 years of age, excluding spasticity caused by cerebral palsy

Prophylaxis for Chronic Migraines

- Not used in combination with calcitonin gene-related peptide (CGRP) inhibitors (e.g., eptinezumab, erenumab, galcanezumab, fremanezumab, etc.); **AND**
- Patient is utilizing prophylactic intervention modalities (i.e., pharmacotherapy, behavioral therapy, or physical therapy, etc.); **AND**
- Patient has 15 or more headache (tension-type-like and/or migraine-like) days per month for at least 3 months; **AND**
  - Patient has had at least five attacks with features consistent with migraine (with and/or without aura) **§**; **AND**
  - On at least 8 days per month for at least 3 months:
    - Headaches have characteristics and symptoms consistent with migraine**§**; **OR**
    - Patient suspected migraines are relieved by a triptan or ergot derivative medication; **AND**
- Patient has failed at least an 8-week trial of any two oral medications for the prevention of migraines (see list of migraine-prophylactic medications below for examples)

Incontinence due to neurogenic detrusor overactivity

- Patient has detrusor overactivity associated with a neurologic condition (i.e., spinal cord injury, multiple sclerosis, etc.) that is confirmed by urodynamic testing; **AND**
- Patient has failed a 1 month or longer trial of two medications from either the antimuscarinic (i.e., darifenacin, fesoterodine, oxybutynin, solifenacin, tolterodine or trospium) or beta-adrenergic (i.e., mirabegron) classes.

Overactive Bladder (OAB)

- Patient has symptoms of urge urinary incontinence, urgency, and frequency; **AND**

- Patient has failed a 1 month or longer trial of two medications from either the antimuscarinic (i.e., darifenacin, fesoterodine, oxybutynin, solifenacin, tolterodine or trospium) or beta-adrenergic (i.e., mirabegron) classes.
- ~~No current, untreated urinary tract infection~~

Severe Primary Axillary Hyperhidrosis

- Patient has tried and failed ≥ 1 month trial of a topical agent (e.g., aluminum chloride, glycopyrronium, etc.); **AND**
  - Patient has a history of medical complications such as skin infections or significant functional impairments; **OR**
  - Patient has had a significant burden of disease or impact to activities of daily living due to condition (e.g., impairment in work performance/productivity, frequent change of clothing, difficulty in relationships and/or social gatherings, etc.)

Chronic Sialorrhea

- Patient has a history of troublesome sialorrhea for at least a 3 month period; **AND**
  - Patient has Parkinson's disease, atypical Parkinsonism, stroke, or traumatic brain injury; **OR**
  - Patient has a severe developmental delay; **OR**
  - Patient has cerebral palsy, other genetic or congenital disorders, or traumatic brain injury; **AND**
    - Patient is at least 2 years of age

Ventral Hernia

- Patient has a large ventral hernia with loss of domain or contaminated ventral hernia; **AND**
- Used preoperatively in patients scheduled to receive abdominal wall reconstruction (AWR)

Migraine-Prophylaxis Oral Medications *(list not all-inclusive)*
• Antidepressants (e.g., amitriptyline, fluoxetine, nortriptyline, etc.) • Beta blockers (e.g., propranolol, metoprolol, nadolol, timolol, atenolol, pindolol, etc.) • Angiotensin converting enzyme inhibitors/angiotensin II receptor blockers (ex. lisinopril, candesartan, etc.) • Anti-epileptics (e.g., divalproex, valproate, topiramate, etc.) • Calcium channels blockers (e.g., verapamil, etc.)
Migraine Features §

Migraine without aura
• At least five attacks have the following:
  ○ Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated)
  ○ Headache has at least two of the following characteristics:
  ▪ Unilateral location
  ▪ Pulsating quality
  ▪ Moderate or severe pain intensity
  ▪ Aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs); **AND**
  ○ During headache at least one of the following:
  ▪ Nausea and/or vomiting
  ▪ Photophobia and phonophobia

Approved Revision: Do Not Implement Until 6/2/21

Migraine with aura

- At least two attacks have the following:
  - One or more of the following fully reversible aura symptoms:
    - Visual
    - Sensory
    - Speech and/or language
    - Motor
    - Brainstem
    - Retinal; **AND**
  - At least two of the following characteristics:
    - At least one aura symptom spreads gradually over ≥5 minutes, and/or two or more symptoms occur in succession
    - Each individual aura symptom lasts 5 to 60 minutes
    - At least one aura symptom is unilateral
    - The aura is accompanied, or followed within 60 minutes, by headache

RENEWAL CRITERIA

- Patient continues to meet universal and indication-specific criteria as identified in Initial Approval Criteria; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: symptoms of a toxin spread effect (e.g. asthenia, generalized muscle weakness, diplopia, blurred vision, ptosis, dysphagia, dysphonia, dysarthria, breathing difficulties, etc.), hypersensitivity reactions, corneal exposure/ulceration, ectropion in patients treated for blepharospasm, etc.; **AND**
- Disease response as evidenced by the following:

Blepharospasms

- Improvement of severity and/or frequency of eyelid spasms

Cervical dystonia

- Improvement in the severity and frequency of pain; **AND**
- Improvement of abnormal head positioning

Upper Limb Spasticity

Decrease in tone and/or resistance, of affected areas, based on a validated measuring tool (e.g., Ashworth Scale, Physician Global Assessment, Clinical Global Impression (CGI), etc.)

Severe primary axillary hyperhidrosis

- Significant reduction in spontaneous axillary sweat production; **AND**
- Patient has a significant improvement in activities of daily living

Prophylaxis for chronic migraines

- Significant decrease in the number, frequency, and/or intensity of headaches; AND
- Improvement in function; AND
- Patient continues to utilize prophylactic intervention modalities (i.e. pharmacotherapy, behavioral therapy, physical therapy, etc.)

Incontinence due to Detrusor Overactivity

- Significant improvements in weekly frequency of incontinence episodes; **AND**
- Patient's post-void residual (PVR) periodically assessed as medically appropriate

Overactive bladder (OAB)

- Significant improvement in daily frequency of urinary incontinence or micturition episodes and/or volume voided per micturition; **AND**
- Patient's post-void residual (PVR) periodically assessed as medically appropriate

Chronic Sialorrhea

- Significant decrease in saliva production

Ventral Hernias

- May not be renewed.

DOSAGE/ADMINISTRATION

INDICATION	DOSE
Cervical Dystonia	The recommended initial total dose for cervical dystonia is 120 units. Initial dose is divided among the affected muscles every 12 weeks or longer, as necessary
Blepharospasm	1.25-5.6 units per injection site, not to exceed 50 units per eye (maximum of 35 units per eye for initial dose), every 12 weeks or longer, as necessary
Upper limb spasticity	The dosage, frequency, and number of injection sites should be tailored to the individual patient based on the size, number, and location of muscles to be treated, severity of spasticity, presence of local muscle weakness, patient's response to previous treatment, and adverse event history with Xeomin. Localization of the involved muscles with electromyographic guidance, nerve stimulation, or ultrasound techniques is recommended. Adults Up to 400 units total, repeated no sooner than every 12 weeks Pediatrics 8 units/kg, divided among affected muscles, up to a maximum dose of 200 units per single upper limb. If both upper limbs are treated, total XEOMIN dosage should not exceed 16 Units/kg, up to a maximum of 400 units, repeated no sooner than every 12 weeks
Chronic Migraine	Up to 200 units divided among the affected muscles every 12 weeks
Severe primary Axillary hyperhidrosis	50 units intradermally per axilla every 16 weeks
Neurogenic bladder/ Detrusor overactivity	Up to 200 units per treatment divided among the affected muscles every 12 weeks

Sialorrhea	Adults 30 units per parotid gland and 20 units per submandibular gland (50 units per each side of the face for a total recommended dose of 100 units per treatment session), repeated no sooner than every 16 weeks Pediatrics: Dosing is based on body weight as noted below and is repeated no sooner than every 16 weeks ▫ 12 kg to <15 kg: 6 units per parotid gland and 4 units per submandibular gland (10 units per each side of the face for a total recommended dose of 20 units per treatment session) ▫ 15 kg to <19 kg: 9 units per parotid gland and 6 units per submandibular gland (15 units per each side of the face for a total recommended dose of 30 units per treatment session) ▫ 19 kg to <23 kg: 12 units per parotid gland and 8 units per submandibular gland (20 units per each side of the face for a total recommended dose of 40 units per treatment session) ▫ 23 kg to <27 kg: 15 units per parotid gland and 10 units per submandibular gland (25 units per each side of the face for a total recommended dose of 50 units per treatment session) ▫ 27 kg to <30 kg: 18 units per parotid gland and 12 units per submandibular gland (30 units per each side of the face for a total recommended dose of 60 units per treatment session)
Ventral Hernia	500 units divided among abdominal muscles injected 2-4 weeks prior to AWR surgery *May not be renewed.*
Note: The recommended maximum cumulative dose for any indication should not exceed 400 Units in a treatment session (unless used for Ventral Hernia).	

LENGTH OF AUTHORIZATION

- Coverage will be provided for six months and may be renewed.
- Preoperative use in Ventral Hernia may NOT be renewed.

DOSAGE LIMITS

Max Units (per dose and over time) [HCPCS Unit]:

Indication	Billable Units	Per # days
Cervical dystonia	200	84
Blepharospasms	100	84
Upper limb spasticity	400	84
Prophylaxis for chronic migraines	200	84
Incontinence due to neurogenic detrusor overactivity	200	84
Overactive bladder (OAB)	100	84
Severe primary axillary hyperhidrosis	100	112
Sialorrhea	100	112
Ventral Hernia	500	N/A

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

1. Xeomin [package insert]. Dessau-Rosslau, Germany; Merz Group Services GmbH; December 2020. Accessed December 2020.
2. Simpson DM, Hallett M, Ashman EJ, et al. Practice guideline update summary: Botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache. Report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology 2016: 86:1-9
3. Grogan P, Robinson A, Chao W, Ford A. Incobotulinumtoxin A for the Preventive Treatment of Chronic Migraine Headaches. Neurology April 8, 2014 vol. 82 no. 10 Supplement P7.188
4. Lakraj AA1, Moghimi N, Jabbari B. Hyperhidrosis: anatomy, pathophysiology and treatment with emphasis on the role of botulinum toxins. Toxins (Basel). 2013 Apr 23; 5(4):821-40. doi: 10.3390/toxins5040821.
5. Pastorelli F, Michelucci R, Plasmati R. A Randomized Controlled Trial Comparing Botulinum Toxin Type A Xeomin ® and Dysport ® for Treatment Of Primary Axillary Hyperhidrosis (P3.021). Neurology April 8, 2014 vol. 82 no. 10 Supplement P3.021
6. Dressler D. Routine use of Xeomin in patients previously treated with Botox: long term results. Eur J Neurol. 2009 Dec; 16 Suppl 2:2-5. doi: 10.1111/j.1468-1331.2009.02877.x.
7. Hampel C, D'Andrea D, Gillitzer R, et al. Comparison of two different Botulinumtoxin A products (Xeomin, Botox) used for detrusor injection in patients with bladder overactivity (BO) – a prospective randomized double-blind study. Paper presented at: the 27th Annual European Association of Urology (EAU) Congress - February 24 - 28, 2012 - Le Palais des Congrès de Paris, Paris, France
8. The International Classification of Headache Disorders, 3rd edition (beta version).Headache Classification Committee of the International Headache Society (IHS) Cephalalgia. 2013 Jul;33(9):629-808.
9. Gormley EA, et al. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: American Urological Association (AUA)/Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU) guideline. April 2019.
10. Schwedt TJ. Chronic Migraine. BMJ. 2014;348:g1416.

11. Modi S, Lowder DM. Medications for migraine prophylaxis. Am Fam Physician. 2006 Jan 1; 73(1):72-8.
12. Pringheim T, Davenport W, Mackie G, et al. Canadian Headache Society guideline for migraine prophylaxis. Can Jneurol Sci. 2012 Mar; 39(2 Suppl 2):S1-S9.
13. Blitzer A, Friedman A, Michel O, et al. SIAXI: IncobotulinumtoxinA for Sialorrhea in Parkinson's Disease, Stroke, and Other Etiologies-Phase III results. Archives of Physical Medicine and Rehabilitation, 2017 Dec. Volume 98, Issue 12, e161.
14. Jost W, Friedman A, Michel O, et al. SIAXI: Efficacy and safety of Xeomin (incobotulinumtoxinA) for the treatment of sialorrhea in Parkinson's disease (PD) and other neurological conditions: Results of a Phase III, placebo-controlled, randomized, double-blind study (S2.007). Neurology Apr 2018, 90 (15 Supplement) S2.007
15. Glaser DA, Hebert AA, Nast A, et al. Topical glycopyrronium tosylate for the treatment of primary axillary hyperhidrosis: Results from the ATMOS-1 and ATMOS-2 phase 3 randomized controlled trials. J Am Acad Dermatol. 2019;80(1):128. Epub 2018 Jul 10
16. American Headache Society. The American Headache Society Position Statement On Integrating New Migraine Treatments Into Clinical Practice. Headache. 2019 Jan;59(1):1- 18. doi: 10.1111/head.13456. Epub 2018 Dec 10.
17. Haider A, Solish N. Focal hyperhidrosis: diagnosis and management. CMAJ. 2005;172(1):69-75.
18. Nawrocki S, Cha J. The Etiology, Diagnosis and Management of Hyperhidrosis: A Comprehensive Review. Part II. Therapeutic Options. J Am Acad Dermatol. 2019 Jan 30. pii: S0190-9622(19)30167-7.
19. Kuo HC, Chen SL, Chou CL, et al. Taiwanese Continence Society clinical guidelines for diagnosis and management of neurogenic lower urinary tract dysfunction. Urological Science, Volume 25, Issue 2, 2014, pp. 35-41
20. Motz BM, Schlosser KA, Heniford BT. Chemical Components Separation: Concepts, Evidence, and Outcomes. Plast Reconstr Surg. 2018 Sep;142(3 Suppl):58S-63S. doi: 10.1097/PRS.0000000000004856.
21. Elstner KE, Read JW, Saunders J, et al. Selective muscle botulinum toxin A component paralysis in complex ventral hernia repair. Hernia. 2019 Apr 4. doi: 10.1007/s10029-019- 01939-3.
22. Merz Pharmaceuticals. Clinical Study to Investigate the Efficacy and Safety of NT 201 Compared to Placebo in the Treatment of Chronic Troublesome Drooling Associated With Neurological Disorders and/or Intellectual Disability (SIPEXI). Available from: https://clinicaltrials.gov/ct2/show/NCT02270736?cond=incobotulinumtoxinA+for+sialorrhea &draw=2&rank=3. NLM identifier: NCT02270736. Accessed December 22, 2020
23. Lexi-Comp Online. (2021). AHFS DI. *AbobotulinumtoxinA*. Retrieved January 20, 2021 from Lexi-Comp Online with AHFS.
24. MICROMEDEX Healthcare Series. Drugdex Drug Evaluations. (2020, December). IncobotulinumtoxinA. Retrieved January 20, 2021 from MICROMEDEX Healthcare Series.

EFFECTIVE DATE 6/2/2021

ID_MRx